Observing the Properties of pH Sensitive Hydrogel Microcapsules

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Introduction

Due the precise control of thickness, layer-by-layer (LbL) deposition of polymeric or large organic molecules has been recognized as a tool to create thin films on surfaces. When these surfaces are micro-sized particles, shells of these organics are created around the substrates. Dissolving the particulate substrate leaves behind a hollow organic shell.[1] Many studies used polymers with opposite charge to use electrostatic attractions to favor self-assembly on the substrates; however, because the particles must cross the zero charge potential the particles may had been unstable resulting in aggregation.

More recently, an alternative mechanism for LBL self-assembly, namely via hydrogen bonds was used for deposition in which the zeta potential was kept away from zero. By this method a poly-(methyl acrylic acid) (PMAA) derived hydrogel was produced which demonstrated swelling behavior above pH 5.5. Swelling occurred when sufficiently high pH ionized carboxylic acid groups breaking hydrogen bonds between acid groups and building up the negative charge on the carboxylate groups which ultimately repelled each other.[2]

In this study we used the same swelling mechanism in an attempt to design a hydrogel capsule that would be stable to a higher pH by using tannic acid, a natural biocompatible molecule. Tannic acid can be seen as a poly-phenol so without carboxylic acid groups, tannic acid must be taken to a higher pH to ionize its phenol groups. Many systems were considered by varying the number of layers deposited, the crosslinking time, and the second component of deposition. Such pH-sensitive capsules when triggered have the ability to rapidly deliver macromolecules and thus have potential applications in biomedical research.

Technical Approach

Deposition on silica microbeads (4.0 +/-0.2 µm) consisted of dispersing the beads in 1mg/ml pH 5 buffered solutions (tannic acid, poly-(vinyl caprolactam) (PVCL), poly-(vinyl pyrrolidone) (PVPON), poly-(ethylene imine) (PEI)) for 15 minutes followed by two washings via centrifuge separation and re-dispersion in buffer. PEI was typically the first layer deposited to neutralize surface charge followed by a layer of tannic acid that would deposit electrostatically. Depending on whether the capsule was to be single component or double component, the next solution introduced would be 0.5% glutaraldehyde solution for a desired time or a neutral polar polymer (PVCL or PVPON) for 15 minutes, respectively. This step and deposition of tannic acid would be executed in an alternating fashion to produce bilayers or crosslinked layers. For double component capsule walls after the desired number of layers is deposited, the tannic acid layers was crosslinked by glutaraldehyde for a desired time and followed by exposure to pH 10 to release PVCL or PVPON. After the layers were crosslinked, the silica cores was dissolved by exposure to 8% hydrofluoric acid for at least two hours and dialyzed for at least 24 hours using Spectra-Por® Float-a-lyzers (mw. 50 kDa, 1ml). The product was dried for observation with SEM (Hitachi S-3400N) and swollen for analysis with CLSM (Zeiss LSM510, Argon Laser, Alexa 488nm) to produce images as seen in figure 1.

Results and Discussion

![Fig. 1. SEM (left) and CLSM (right) images of two-component capsules composed of 4 bi-layers of tannic acid and PVPON (mw. 55kDa) crosslinked by glutaraldehyde for 5 min.](image)

Using SEM to observe morphology we determined that the minimum number of layers needed to form capsules was four crosslinked layers of tannic acid for single component walls and two bilayers of tannic acid and PVPON for double component walls. The stability of the capsule walls seemed to be dependent on wall thickness and extent of hydrogen bonding. After the capsule formation was confirmed with SEM, swelling behavior would be tested and observed with CLSM by washing the capsules in different pH buffers three of more times. When using CLSM to observe pH-response, most systems did not swell noticeably even to pH 10. This may be due to possibility that PEI as a polycation countered the driving force of tannic acid to swell, that the neutral polar polymer was not released, and that the crosslinking density was too high. When the crosslinking density is too high, not only does the network become too rigid to stretch but also the tannic acid functionality is compromised and cannot ionize sufficiently for the swelling mechanism to occur.

Conclusion

Because capsules produced thus far have not noticeably swollen to pH change, further study needed. Future experiments to increase swelling behavior may involve decreasing the crosslinking density by decreasing crosslinking time, decreasing the crosslinker concentration, and increasing the crosslinker chain segment length.

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Reference
